

REMARKS

Favorable reconsideration of this application is respectfully requested.

This application relates to synthetic saccharidic compounds which are useful in the treatment of thrombosis, to pharmaceutical compositions containing the compounds, to the use of the compounds to detect and treat thrombosis and to the process for making these useful synthetic compounds.

There are now 46 claims in this application, claims 42-48, 86-124. Claims 83-85 have been cancelled as being directed to a non-elected invention.

The newly presented compound claims have been amended in response to the outstanding Office Action and correspond to the prior claims according to the following table.

<u>New claim</u>	<u>Prior claim</u>
89	52
90	53
91	54
92	55
93	56
94	57
95	58
96	59
97	60
98	61
99	62
100	63
101	64
102	65

103	66
104	67
105	68
106	41
107	69
108	70
109	71
110	72
111	73
112	74
113	75
114	76
115	77
116	78
117	79
118	80
119	81
120	82
121	49
122	50
123	51
124	-

Claims 42, 52, 54, 56, 58, 60-61, 63-82 and 86-88 were rejected under 35 USC 112, second paragraph as being functional, indefinite and alternative in the use of the terms "substituted" and "a precursor".

The term "precursor" no longer appears in the claims.

The term "substituted" has been amended to "phenyl-substituted". Basis is found in the benzyl and trityl (triphenylmethyl) groups disclosed, for example, in Figure 29, compound No. 164.

Accordingly, applicants submit that the newly presented claims are in conformance with the requirements of 35 USC 112.

Claims 49-82 were rejected under 35 USC 102(a),(b),(e) and (f) as anticipated by or, in the alternative under 35 USC 103 as obvious over each of the patents to Lormeau et al.,

'662, '758 and '770. The Examiner states that "each of the patents discloses heparin fractions of di-, tri- and oligosaccharides and further disclose pharmaceutical compositions thereof and their use in a method for treating thrombosis. The instant compounds, compositions and methods are deemed to be anticipated thereby or prima facie obvious therefrom". This rejection is respectfully traversed.

The claimed compounds of the instant invention are individual synthetic compounds.

In contrast, the heparin fractions which are disclosed in the cited Lormeau et al patents are just that, fractions of heparin which contain mixtures of compounds having different chain lengths and different structures. The heparin fractions are obtained by the depolymerization or fractionation of naturally occurring heparin.

The di-, tri- and oligosaccharides disclosed in the Lormeau patents are not synthetically prepared. The cited references accordingly do not disclose all the "elements" or features claimed in the instant application. Thus, the compounds claimed herein are not anticipated by the Lormeau et al patents.

The claimed compounds of the instant application also are not taught or suggested by the cited Lormeau et al patents. There is no teaching or suggestion of the organic synthesis of the claimed compounds. There is no teaching or

suggestion of the isolation of individual pure compounds for any use.

Claims 89-96, and 98-99 are drawn to intermediate compounds of the process claimed herein. There is no suggestion of these intermediates in the Lormeau patents.

Of the individual oligosaccharide chains listed by the Lormeau patents, for example, the passage in '662 at column 5, very few of the saccharide chains were isolated as pure compounds. See Example 4, column 17 where the hexasaccharide obtained by chromatography was impure.

Even when an oligosaccharide was isolated, the unexpected properties of the instant claimed compounds can be seen, for example, in the comparison of the anti-Xa (Yin-Wessler) activity disclosed. An oligosaccharide of the prior art to which the pentasaccharidic structure DEFGH is attributed by the patentee is disclosed to have anti-Xa (Yin-Wessler) activity of over 400 ui/mg ('662, column 18, lines 33-37). In contrast, a synthetic pentasaccharide of the instant application has an anti-Xa activity equal to or greater than 2,000 u/mg (specification p. 46, lines 14-16).

Applicants submit that the instant claimed synthetic pure compounds are not obvious to one skilled in the art having the cited Lormeau et al patents before him.

Claims 42-48, 86 and 87 are rejected under 35 USC 103 as being unpatentable over each of the patents to Szarek et al,

Nair et al, the PCT French patent or the Kochetkov et al reference and claim 88 is rejected under 35 USC 103 as being unpatentable over each of the Szarek et al, Nair et al, PCT French patent and Kochetkov et al in combination with the Tovey et al and Curtin et al references. These rejections are respectfully traversed.

The Examiner maintains that it would still appear to be obvious to prepare other di-, tri-, oligo, etc, saccharides from the prior art processes to any person of ordinary skill in the art having the above references before him.

The cited references do not teach or suggest the instant claimed sequence of steps utilized to obtain the desired compounds. There is no teaching or suggestion of the condensation of a uronic acid with a glucosamine. One skilled in the art would have no knowledge of the reactivity of the glucosamine moiety. It would not be known how the amino group would influence the stereochemistry at the C 1 position sterically adjacent to the amino group. In this unpredictable field of chemistry one skilled in the art would not be able to predict the stereochemistry of the condensation having the cited references at hand. Accordingly, applicants submit that the claimed process is not obvious from the cited prior art.

In view of the above remarks and the amendments to the claims applicants submit that this application is in condition for allowance. Favorable reconsideration is respectfully requested.

Should the Examiner believe that a telephone call to the undersigned or Gerard J. Weiser, attorney of record, would favorably advance the prosecution of this application or narrow any outstanding issues, she is respectfully invited to call at the telephone number indicated below.

Respectfully submitted,

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Dec 29, 1986
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